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47 (A) NAME/KEY: CDS (B) LOCATION: 51..161 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9: GGGGTGGGAG GGCACGTGGA TGGGACTCAC CTTCTCCCAC TACCCCCGAG GAC TGG Asp Trp GTC ATC GCC CCC CAA GGC TAC TCA GCC TAT TAC TGT GAA 9GG GAG TGC Val Ile Als Pro Gin Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys TEC TTC CCG CTG GAC TCC TGC ATG AAC GCC ACC AAC CAC GCC ATC CTG Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala Ile Leu 30 CAG TCC CTG GTCAGTACCT C Gln Ser Leu (2) INFORMATION FOR SEQ ID NO:10: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 37 amino acids (B) TYPE: amino acid (D) TOPOLOGY: linear (ii) MOLECULB TYPE: protein (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10: Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn Ala Thr Asn His Ala 30 20 Ile Leu Gla Ser Leu 35 (2) INFORMATION FOR SEQ ID NO:11: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 119 base pairs (B) TYPE: nucleic scid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

45	/
(iii) HYPOTHETICAL: NO	
(vi) ORIGINAL SOURCE: (A) ORGANISM: Bos taurus	
(vii) IMMEDIATE SOURCE:  (A) LIBRARY: Bovine genomic  (B) CLONE: Lambda 9800-10	
(viii) POSITION IN GENOME: (C) UNITS: bp	
(ix) FEATURE: (A) NAME/KBY: exon (B) LOCATION: 30199	
(ix) FEATURE: (A) NAME/KEY: intron (B) LOCATION: 129	
(ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 30179	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:	
TGCCCGCTGC CCCCCCCCC CCCCCCCAG GTG CAC CTG CTG AAG CCG CAC GCG  Val His Leu Leu Lys Pro His Als  1  5	53
GTC CCC AAG GCG TGC TGC GCG CCC ACC AAG CTG AGC GCC ACT TCC GTG Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr Ser Val  10 15 20 25	10
CTC TAC TAC GAC AGC AGC AAC GTC ATC CTG CGC AAG CAC CGC AAC Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His Arg Asn 30 36 40	149
ATG GTG GTC CGC GCC TGC GGC TGC CAC TGA GGCCCCAACT CCACCGGCAG  Mot Val Val Arg Ala Cys Gly Cys His  45  50	19
(2) INFORMATION FOR SEQ ID NO:8:	
(i) SEQUENCH CHARACTERISTICS:  (A) LBNoTH: 50 amino scids  (B) TYPE: amino scid  (D) TOPOLOGY: linear	
(ii) MOLECULE TYPE: protein	

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'557 patents may claim priority dates t April 8, 1988, it is understood that the hOP2 disclosure of '683 and '557 upon which the Examiner relies is not found in the applications having earlier priority dates claimed in '683 and '557. Rather, it is Applicants understanding that the hOP2 disclosure was set forth in USSN 599,543 filed October 18, 1990. (See document "BM" WO92/07073 listed on page 2 of the Information Disclosure Statement). It is therefore submitted that the claimed invention is not anticipated by the '683 or '557 patents.

## Rejections Under 35 U.S.C. §103

Claims 1, 2 and 26-29 are rejected as being unpatentable over US 5,011,691 in view of Zoller et al. The '691 patent is cited for disclosure of bone morphogenic proteins and amino acid sequence alignment of various homologous osteogenic proteins showing what regions are conserved. The Examiner contends that it would have been obvious to one skilled in the art to substitute Lys for Gln in the OP1 sequence in Figure 18-1 having the same sequence in Figure 18-3 as "c" in claim 1 using the techniques of Zoller et al. or other conventional techniques to obtain a mutein having the osteogenic activity of OP1. It is further contended that it would have been obvious to use such muteins in compositions.

Claim 2 has been deleted and claims 1 and 26-29 have been amended. The claims as amended characterize the BMP-8 protein by each of the sequences of parts (i)-(iii). Furthermore the BMP proteins belong to a supergene family based on homologies. The OP-1 sequence of '691 is homologous with BMP-7, a member of this family of proteins. The '691 patent does not, however, teach the presently claimed BMP-8 protein, nor in fact that a BMP-8 protein

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Page 2

Page 23 line 26, after "Tyr" insert -- (SEQ ID NO:20)--.

Page 23, line 29, after "Tyr" insert -- (SEQ ID NO:21)--.

Page 24 line 5, after "Lys" insert -- (SEQ ID NO:22)--.

Page 24, line 8, after "Lys" insert -- (SEQ ID NO:23)--.

Page 24 line 11, after "Lys" insert -- (SEQ ID NO:24)--.

Page 24, line 14, after "Lys" insert --(SEQ ID NO:25)--.

Page 24, line 18, after "Lys" insert -- (SEQ ID NO:26)--.

Page 24, line 20, after "Lys" insert -- (SEQ ID NO:27)--.

Page 24, line 29, after "Glu" insert -- (SEQ ID NO:28)--.

Page 24, line 30, after "Lys" insert -- (SEQ ID NO:29)--.

Page 24/line 31, after "Glu" insert -- (SEQ ID NO:30)--.

Page 24 line 32, after "Lys" insert -(SEQ ID NO:31)--.

Page 24, line 33, after "Lys" insert -- (SEQ ID NO:32)--.

Page 24, line 34, after "Gln" insert -- (SEQ ID NO:33)--.

Page 26, line 1, after "ANG" insert -- (SEQ ID NO:34)--.

Page 26, line 3, after "ARC" insert -- (SEQ ID NO:35)--.

Page 26, lines 5, after "TNG" insert -- (SEQ ID NO:36)--.

Page 26, line 7, after "TRC" insert -- (SEQ ID NO:37)--.

Page 26 tine 20, after "NAC" insert -- (SEQ ID NO:38)--.

Page 28, line 9, after "TAC" insert -- (SEQ ID NO:39)--.

Page 30, line 1, after "NCA" insert -- (SEQ ID NO:40)--.